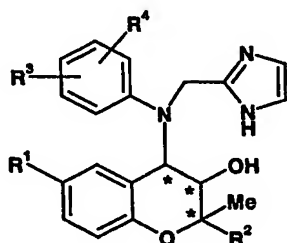


WHAT IS CLAIMED IS :

1. (currently amended) Benzopyran derivatives substituted with secondary amines including imidazole by the following formula 1, their stereochemical isomers and their
5 pharmaceutically acceptable salts.

FORMULA 1



Wherein,

R¹ represents H, CN, NO₂ or NH₂,

10 R² represents $\begin{array}{c} \text{OR}^a \\ | \\ \text{CH} \\ | \\ \text{OR}^a \end{array}$ wherein R^a represents straight or branched alkyl group of C₁-C₄,

R₃ and R₄ are independent each other and represent H, Cl, Br, F, alkyl group of C₁-C₃, OR^b, CF₃, OCF₃, NO₂, or CO₂R^b; R^b represents H or alkyl group of C₁-C₃,

15 and * represents the chiral center.

2. Benzopyran derivatives substituted with secondary amines including imidazole, their stereochemical isomers and their pharmaceutically acceptable salts according to claim 1,
20 wherein the compound of formula 1 is selected from the

group consisting of:

1) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-
2-methyl-6-nitro-4-[N-(4-chlorophenyl)-
N-(1H-imidazol-2-ylmethyl) amino]-2H-1-benzopyran;

5 2) (2S,3R,4S)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-
2-methyl-6-nitro-4-[N-(4-chlorophenyl)-
N-(1H-imidazol-2-ylmethyl) amino]-2H-1-benzopyran;

3) (2R,3R,4S)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-
2-methyl-6-nitro-4-[N-(4-chlorophenyl)-
10 N-(1H-imidazol-2-ylmethyl) amino]-2H-1-benzopyran;

4) (2R,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-
2-methyl-6-nitro-4-[N-(4-chlorophenyl)-
N-(1H-imidazol-2-ylmethyl) amino]-2H-1-benzopyran;

5) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-
15 2-methyl-6-nitro-4-[N-(4-trifluoromethylphenyl)-
N-(1H-imidazol-2-ylmethyl) amino]-2H-1-benzopyran;

6) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-
2-methyl-6-nitro-4-[N-(4-methoxyphenyl)-
N-(1H-imidazol-2-ylmethyl) amino]-2H-1-benzopyran;

20 7) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-
2-methyl-6-nitro-4-[N-(4-trifluoromethoxyphenyl)-
N-(1H-imidazol-2-ylmethyl) amino]-2H-1-benzopyran;

8) (2S,3S,4R)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-
2-methyl-6-nitro-4-[N-(4-bromophenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

9) (2*S*, 3*S*, 4*R*)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-
2-methyl-6-nitro-4-[*N*-(2,4-dimethylphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

5 10) (2*S*, 3*S*, 4*R*)-3,4-dihydro-2-dimethoxymethyl-3-
hydroxy-2-methyl-6-nitro-4-[*N*-(2-isopropylphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

 11) (2*S*, 3*S*, 4*R*)-3,4-dihydro-2-dimethoxymethyl-3-
hydroxy-2-methyl-6-nitro-4-[*N*-(2,3-dimethylphenyl)-

10 *N*-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

 12) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-
hydroxy-2-methyl-6-nitro-4-[*N*-(2,3-dimethylphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

 13) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-
15 hydroxy-2-methyl-6-nitro-4-[*N*-(4-bromophenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

 14) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-
hydroxy-2-methyl-6-nitro-4-[*N*-(4-methoxyphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

20 15) (2*S*, 3*S*, 4*R*)-3,4-dihydro-2-dimethoxymethyl-3-
hydroxy-2-methyl-6-nitro-4-[*N*-(4-fluorophenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

 16) (2*S*, 3*S*, 4*R*)-3,4-dihydro-2-dimethoxymethyl-3-
hydroxy-2-methyl-6-nitro-4-[*N*-(2-methoxyphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

17) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[*N*-(2-isopropylphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

5 18) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[*N*-(2-methoxyphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

19) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[*N*-(3-chlorophenyl)-

10 *N*-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

20) (2*S*, 3*S*, 4*R*)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[*N*-(3-chlorophenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

21) (2*R*, 3*R*, 4*S*)-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-6-nitro-4-[*N*-(4-trifluoromethoxyphenyl)-

15 *N*-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

22) (2*S*, 3*S*, 4*R*)-6-cyano-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-4-[*N*-(4-chlorophenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

20 23) (2*R*, 3*R*, 4*S*)-6-amino-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-4-[*N*-(4-chlorophenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

24) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-4-[*N*-(4-chlorophenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

25) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-
3-hydroxy-2-methyl-4-[*N*-(4-trifluoromethylphenyl)-
N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

5 26) (2*R*, 3*R*, 4*S*)-6-amino-3,4-dihydro-2-dimethoxymethyl-
3-hydroxy-2-methyl-4-[*N*-(4-trifluoromethoxyphenyl)-
N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

27) (2*R*, 3*R*, 4*S*)-6-amino-3,4-dihydro-2-dimethoxymethyl-
3-hydroxy-2-methyl-4-[*N*-(2,3-dimethylphenyl)-

10 *N*-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

28) (2*R*, 3*R*, 4*S*)-6-amino-3,4-dihydro-2-dimethoxymethyl-
3-hydroxy-2-methyl-4-[*N*-(4-methoxyphenyl)-
N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

29) (2*R*, 3*R*, 4*S*)-6-amino-3,4-dihydro-2-dimethoxymethyl-
15 3-hydroxy-2-methyl-4-[*N*-(4-bromophenyl)-
N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

30) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-
3-hydroxy-2-methyl-4-[*N*-(2,3-dimethylphenyl)-
N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

20 31) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-
3-hydroxy-2-methyl-4-[*N*-(2-methoxyphenyl)-
N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

32) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-
3-hydroxy-2-methyl-4-[*N*-(4-methoxyphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

33) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-4-[*N*-(2,4-dimethylphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

5 34) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-4-[*N*-(2-isopropylphenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

35) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-4-[*N*-(4-trifluoromethoxyphenyl)-

10 *N*-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran;

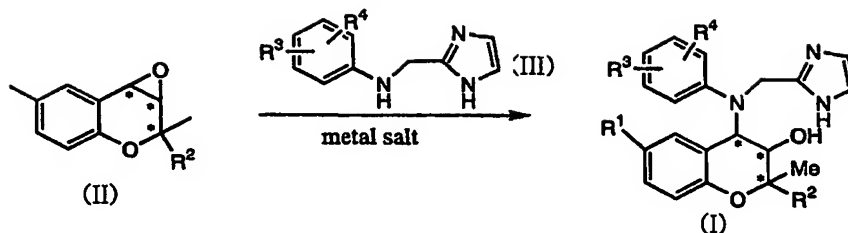
36) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-3-hydroxy-2-methyl-4-[*N*-(4-bromophenyl)-

N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran; and

37) (2*S*, 3*S*, 4*R*)-6-amino-3,4-dihydro-2-dimethoxymethyl-15 3-hydroxy-2-methyl-4-[*N*-(4-fluorophenyl)-
N-(1*H*-imidazol-2-ylmethyl) amino]-2*H*-1-benzopyran.

3. (previously amended) A process for preparing the benzopyran derivatives substituted with secondary amines including imidazole of claim 1, comprising the step of reacting an epoxide compound (II) with a secondary amine compound including imidazole (III) in the presence of a metal salt in an reaction solvent to obtain a compound (I), as described in scheme 1.

Scheme 1



Wherein R₁, R₂, R₃, R₄ * and n are each defined as above claim 1, the metal salt is selected from the group consisting of Mg(ClO₄)₂, CoCl₂, LiClO₄, NaClO₄, CaCl₂, ZnCl₂, LiBF₄ and Zn(Tf)₂, and the reaction solvent is selected from the group consisting of acetonitrile, tetrahydrofuran and dimethylformamide.

4. (previously deleted)

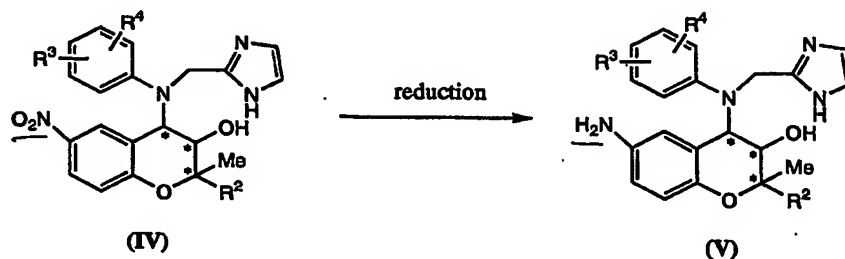
5. (previously deleted)

6. A process for for preparing the benzopyran derivatives substituted with secondary amines including imidazole of claim 1, comprising the step of

1) reduction of the nitro compounds (IV) by hydrogenation using metal catalysts such as platinum, palladium, palladium on carbon (Pd/C), Raney-nickel, etc. in a suitable solvent, to obtain the amino compound (V) as described in scheme 4, below; or

2) reduction of the nitro compounds (IV) using an reducing agent in the presence of CuSO_4 , $\text{Cu}(\text{OAc})_2$, CoCl_2 , SnCl_2 or NiCl_2 , to obtain the amino compound (V) as described in scheme 4, below.

5 Scheme 4



Wherein R^2 , R^3 , R^4 and * are each defined as above claim 1.

10

7. The process according to claim 6, wherein the reducing agent is NaBH_4 .

8. Pharmaceutical compositions pharmacologically useful for
15 treatment of cancer, diabetic retinopathy, and rheumatoid arthritis by suppressing angiogenesis, which contain the benzopyran derivatives substituted with secondary amines including imidazole of claim 1 or their pharmaceutical acceptable salts as an active ingredient.

20

9. Pharmaceutical compositions pharmacologically useful as neuroprotectives for prevention and treatment of infant

asphyxia, glaucoma, diabetic neuropathy, and head trauma, which contain the benzopyran derivatives substituted with secondary amines including imidazole of claim 1 or their pharmaceutical acceptable salts as an active ingredient.

5

10. Pharmaceutical compositions pharmacologically useful as anti-oxidants for prevention and treatment of neurodegenerative diseases including aging, senile dementia, and atherosclerosis, which contain the benzopyran derivatives substituted with secondary amines including imidazole of claim 1 or their pharmaceutical acceptable salts as an active ingredient.

11. (currently deleted)